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During the second year of this study, the imaging technology of Dynamic Functional Optical Mammoscopy (DFOM) has continued to be used to scan patients scheduled for biopsy of breast lesions. These patients were scheduled for core or excisional breast biopsy on the basis of equivocal mammographic and ancillary clinical findings within ACR BI-RADS™ categories 3 or 4. Analysis of test results of 117 patients showed that DFOM modality detected cancer in 13 of the 15 patients in whom biopsies confirmed malignant lesions, giving a sensitivity of 87%. DFOM also correctly identified 79 of 102 benign lesions giving a specificity of 77%. In clinical practice, the adjunctive use of DFOM would have decreased the percentage of biopsies that turn out to be benign from 102/117 (87%) to 23/117 (20%). The negative predictive value, the chance that a negative DFOM result truly indicates a benign lesion, was 79/81 (98%) for the cases included thus far.

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INTRODUCTION

The imaging technology of Dynamic Functional Optical Mammoscopy (DFOM) is a breast scan based upon transmission/absorption of infrared light, which measures the dynamic patterns of breast reactivity of physiological states in response to soft pressures. The DFOM modality focuses on a *functional* rather than a morphological image, expressed by the dynamic patterns of tissue reactivity after mild compression is charted. Pilot study results suggested that this innovative DFOM imaging technique has the potential to determine which mammographically and clinically indeterminate lesions are benign vs. carcinoma and distinguish those lesions that could avoid biopsy. The purpose of the study reported here is to extend the preliminary results of the pilot studies at Columbia Presbyterian Medical Center, using DFOM performed between mammography and biopsy to further evaluate the efficacy of DFOM in evaluation of breast lesions. Our report for the year ending September 30, 2000 summarized results on 117 patients scanned between June 1, 2000 and September 30, 2000. This second year report continues in the direction of Task 2 in acquiring additional patients and begins to focus on the analysis of dynamic data thus acquired, in terms of blood profusion patterns that characterize lesions and improved specificity.

BODY

A total of 189 patients scheduled for biopsy were scanned with the identical protocol between October 1, 2000 and September 30, 2001. The study was performed on women scheduled for core or excisional breast biopsy on the basis of equivocal mammographic and ancillary clinical findings within ACR BI-RADS™ categories 3 or 4. Women who met the selection criteria were enrolled from the normal caseload from both screening and diagnostic mammography. Each woman signed an informed consent prior to being scanned.

Each woman was scanned by a trained technologist prior to biopsy. The scan procedure required approximately 5 minutes. During examination, the breast was placed in the soft breast holder of the system. The breast was then softly compressed by a thin transparent silicone rubber membrane using an applied pressure of approximately 10 mm Hg. For each scan, the breasts were symmetrically centered on the illuminator with special effort made to keep the lesion appearing on the mammogram within the field of view.

When the breast was correctly positioned, illumination adjustment and image recording took place following the requirements of the pressure profile. Optical illumination was provided by an array of red light emitting diodes (LEDs) attached to the bottom surface of the soft breast holder. Light transmitted through the breast was recorded as a temporal sequence for approximately 30 - 45 seconds by a highly sensitive digital CCD camera. The image sequences were accumulated in digital memory and processed by proprietary software to accentuate differences in the temporal variations of intensity between normal/benign and malignant tissue.

The scans were read by an experienced reader trained in interpreting the scans. Results were reported as either a recommendation for biopsy or a recommendation that the woman be sent to interval follow-up.
Recommendations on the basis of DFOM were compared to pathology reports of malignant or benign which were used as the gold standard. Sensitivity, specificity, and negative predictive value were calculated.

Table 1 gives the patient accounting for the 189 patients reported on here.

TABLE 1 – Patients Scanned October 1, 2000 – September 30, 2001

Excluded patients*	= 36
Unacceptable scans**	= 36
Interpreted scans	= 117
Total scans performed	= 189

*Patients who did not meet the selection criteria for the development study protocol.
**Patients whose scans were not acceptable to be interpreted.

Table 2 presents the reasons for scans determined to be unacceptable.

TABLE 2 – Unacceptable Scans

Lesion subareolar or located where it cannot be properly illuminated	= 1
Inadequate illumination in area of pathology	= 1
Device related	= 0
Incorrect illumination	= 1
Not enough breast tissue in holder	= 0
Excessive patient movement	= 5
No case report form	=28
Total	=36

Table 3 presents patient demographics of race and age.

TABLE 3 – Patient Demographics

Race	
White	= 69
African American	= 15
Hispanic White	= 55
Hispanic Black	= 16
Hispanic	= 2
Asian	= 1
Other	= 3
No data	= 28
Total	= 189

AGE: Average = 53
Range = 20-91

Table 4 presents the reasons for excluded scans.

TABLE 4 – Excluded Scans

Lesion subareolar or located where it cannot be properly illuminated	= 14
Previous surgery in the ipsilateral breast	= 1
BI-RADs 5 lesion	= 2
Post-menopausal with a palpable lesion	= 1
Not all records available	= 13
Age >74	= 3
Small breast that cannot be properly illuminated	= 1
Patient unable to remain still	= 1
Total	= 36

Table 5 presents the results of scan interpretation.

TABLE 5– Results of 117 Patients Scheduled for Biopsy

		Pathology		
		Malignant	Benign	Total
DFOM Recommendation	Biopsy	13	23	36
	Interval Follow-Up	2	79	81
	Total	15	102	117

Sensitivity:	13/15 (87%)
Specificity:	79/102 (77%)
Negative Predictive Value (NPV):	79/81 (98%)

The analysis of test results on the 117 patients with interpreted scans shows that the DFOM detected cancer in 13 of the 15 patients in whom biopsies confirmed malignant lesions ("true positives"). This results in a sensitivity of 87%. The system also correctly identified 79 of 102 benign lesions ("true negatives"). In other words, the specificity of the DFOM was 79/102 (77%).

Modification of Task 3

During the past year our discussions with personnel at DOBI Medical Systems suggested that we need better analysis of the current data before proceeding with an evaluation of screening high risk women. Specifically, due to subtle problems in the acquisition of dynamic data we recognized that sensitivity and specificity are not where they could be. Thus during the final year of this project, we propose to focus on improving the quality of the data in the following areas:

1) *Artifact Removal* - This task involves non-linear filtering to remove imaging artifacts caused by near surface structures such as vessels, tattoos and skin pigmentation. These objects create contrast in our images that are undesirable. Our goal is to apply a filter algorithm that would remove these artifacts while preserving contrast created by deep lesions.

2) *Motion Detection* - Patient motion has been an ongoing problem with DOBI Medical's imaging modality. Motion can be generated by a number of ways, such as normal respiratory movement, heartbeats, the patient moving due to stress. We can estimate this motion by looking at edge effects. We will apply a motion detection algorithm to estimate the amount of movement during acquisition.

3) *Simplified Tumor Model* - DOBI Medical has developed a rather complex model for the hemodynamics in a tumor. The model has not been validated and could take a significant effort to quantify the parameters associated with this model. We would like to jointly work with the technical staff at DOBI on a simplified model that could be verified.

4) *Complex Data Presentation* - DOBI Medical needs better ways to present complex data to the physician. Currently we produce a static image of intensity and a cine loop of dynamic intensity over time. In the future we will be presenting such parameters as a map of change in absorption, a map of intensity, a map of direction vectors associated with increasing or decreasing absorption. We would like to jointly work with DOBI on presenting these complex data sets to physicians in a more intuitive presentation format.

These tasks will a continuation of the joint effort between Columbia University and DOBI Medical Systems. Dr. John Gardner, Vice President of Technology at DOBI will supervise the DOBI effort. To assist with these studies at Columbia, we would like Dr. Andrew Laine, Associate Professor of Biomedical Engineering and Radiology to become a collaborator for this phase of the project. Dr. Laine would supervise a graduate research assistant during this period. **No additional funds are requested to complete the project with this modification.** Remaining funds in the original budget are sufficient to carry out the proposed new goals of Task 3.

KEY RESEARCH ACCOMPLISHMENT

(1) The effectiveness of the DFOM in discriminating between benign and malignant breast lesions has been further evaluated and the preliminary results have been corroborated.

(2) The results reported here show an improvement in sensitivity, specificity, and negative predictive value over those reported in the last annual report.

(3) However, we determined that the sensitivity was not sufficient to merit the screening study for high-risk women as planned in Task 3 of the original Statement-of-Work. We need to overcome existing acquisition and analysis problems before going forward with such a study. We met with engineers and management of Dobi Medical Systems in order to identify the most promising methods of improving sensitivity and specificity of DFOM. The outcome of these discussions resulted in our decision to investigate existing problems related to (a) Artifact removal, (b) Motion detection, (c) Tumor profusion models, and (d) Presentation of temporal data.

REPORTABLE OUTCOMES

We expect to publish our results during the next (final year) of this study. To determine the performance of this modality as accurately as possible, we want to include as many patients as possible within the period of study before publishing results.

CONCLUSIONS

The indications of effectiveness of this new modality are very encouraging. The results reported above indicate that the adjunctive use of the DFOM in clinical practice would have decreased the percentage of biopsies that turn out to be benign from 102/117 (87%) to 23/117 (20%). The negative predictive value, the chance that a negative DFOM result truly indicates a benign lesion, is 79/81 (98%).

The next phase of this project will focus on completing the modified Task 3 and will carry out a final analysis which will be included in our final report next year (Task 5).

REFERENCES

None.